## WORLD INTELLECTUAL PROPERTY ORGAN. International Bureau

C12N 15/12, C07K 13/90 C12N 5/10, A61K 37/02 G01N 33/68 (21) International Application Number:



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

WO 94/11502 (51) International Patent Classification 5: (11) International Publication Number: **A2** (43) International Publication Date: 26 May 1994 (26.05.94)

PCT/GB93/02367

17 November 1993 (17.11.93) (22) International Filing Date:

(30) Priority data: 17 November 1992 (17.11.92) GB 9224057.1 GB 8 March 1993 (08.03.93) 9304677.9 8 March 1993 (08.03.93) GB 9304680.3 GB 28 May 1993 (28.05.93) 9311047.6 2 July 1993 (02.07.93) GB 9313763.6 3 August 1993 (03.08.93) GB 9316099.2 15 October 1993 (15.10.93) GB 9321344.5

(71) Applicant (for all designated States except US): LUDWIG INSTITUTE FOR CANCER RESEARCH [GB/GB]; St. Mary's Hospital Medical School, Norfolk Place, Paddington, London W2 1PG (GB).

(72) Inventors; and

(72) inventors; and
(75) inventors/Applicants (for US only): MIYAZONO, Kohei
[JP/SE]; Flogstavägen 63D, S-752 63 Uppsala (SE).
DIJKE, Peter, Ten [NL/SE]; Flogstavägen 25C, S-752
63 Uppsala (SE). FRANZEN, Petra [SE/SE]; Lindsbergsgatan 15b, S-752 40 Uppsala (SE). YAMASHITA, Hidetoshi [JP/SE]; Flogstavägen 33A, S-752 63 Uppsala (SE). HELDIN, Carl-Henrik [SE/SE]; Hesselmans väg 35, S-752 63 Uppsala (SE).

(74) Agent: GILL JENNINGS & EVERY; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB).

(81) Designated States: AU, CA, JP, KR, NZ, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published

Without international search report and to be republished upon receipt of that report.

(54) Title: ACTIVIN RECEPTOR-LIKE KINASES, PROTEINS HAVING SERINE THREONINE KINASE DOMAINS AND THEIR USE

> C C C V cons . 22 htgfer-II idtlygkgrfaeytaalkontseofetvavkifpydhyasworkdifsdinlichenilof ILLEI KARGREGGYMKAQLASI ----- DEVAVKI KPLODKOS WOSEREI ESTPONOHEMILLOF BACKR-IIB LLEVKARGRECCVMDQLLN----EYVAVKIFPIQDKQSWQNEYEVYSIPQHDHELLQF BACKR-II LTHRVCSGRFGNVSRCDYRG-----EAVAVKVFNAIDEPAFHKEIEIFETRMLRHPMVLRY daf-1. 11 III subdomains

> htgfer-ii litaferktelgkomlitafhakonlge/litrhviswedlrhvgsslarglshlhsdhtp-c IAAEKROSHLEVEIMLITAFHDKOSLIDYLKOHIITHNELCHVAETHSRGISYLHEDVFMCR BACKR-IIB IGAEKROTSVDVDLMLITAFHEKGSLSDFLKANVVSWNELCHIAETHARGLAYLHEDI POLI mactr-II igsdrydtgfytelmlyieyhpsgslhdfllentynietyynlarstasglaflhingiggsk def-1 subdomains

DLK N DFG cons.aa -GRPRIPIVIRDLESSNILVRIDLTCCLCDFGLSLRL---GPYSSVDDLANSGQVGTARYMAP bTGFBR-11 GECHKPSIAHRDFKSRIVLLKSDLTAVLADFCLAVRF···EPGKPPGD··THCQVGTRXTIQAP MACTR-IIB ·DGHEPALSHEDIKSTRVLLKHRUTACLADFGLALKF···BAGKSAGD··THCQVGTRRYFAP BACKR-II · ESNKPAMAHRDIKSINTHYKNDLITCAI CDLGLSLSKPEDAASDIIAN · · ENYKCGTVRYLAP daf-1 VII VIII subdomains

## (57) Abstract

A new receptor family has been identified, of activin-like kinases. Novel proteins have activin/TGF-B-type I receptor functionality, and have consequential diagnostic/therapeutic utility. They may have a serine/threonine kinase domain, a DFKSRN or DLKSKN sequence in subdomain VIB and/or a GTKRYM sequence in subdomain VIII.

Ę ŧ. E W m 12

10